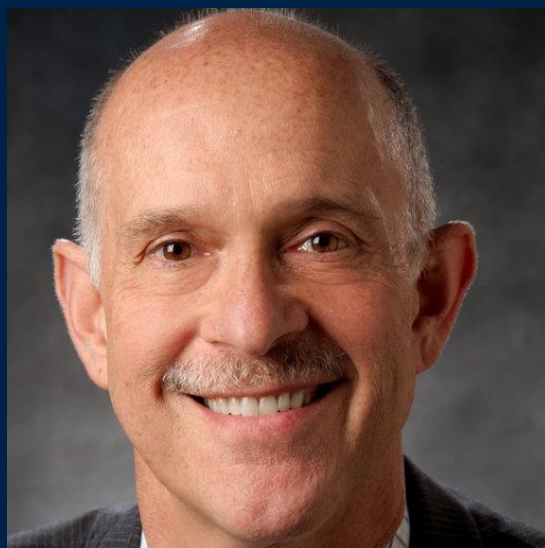


100 Years Since 1918: Are We Ready for the Next Pandemic?

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Influenza Division

Centers for Disease Control and Prevention
August 29, 2018



Toby Merlin
1952 - 2018

Significant Annual Burden of Influenza in Humans



United States



Global

12,000 – 56,000

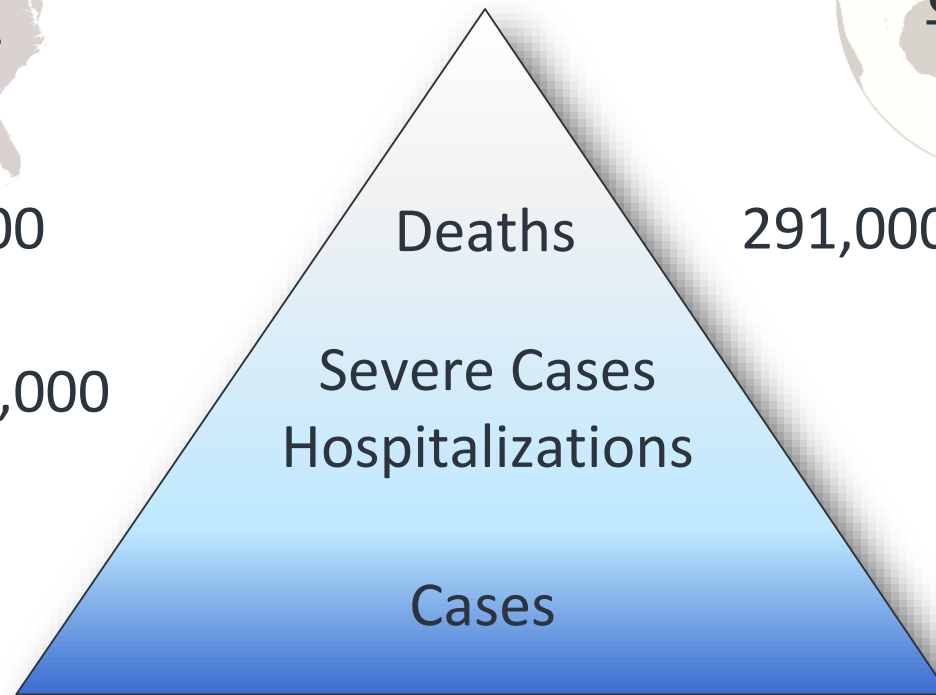
291,000 – 646,000

140,000 – 710,000

3M to 5M

9.2M – 35.6M

1.0 B

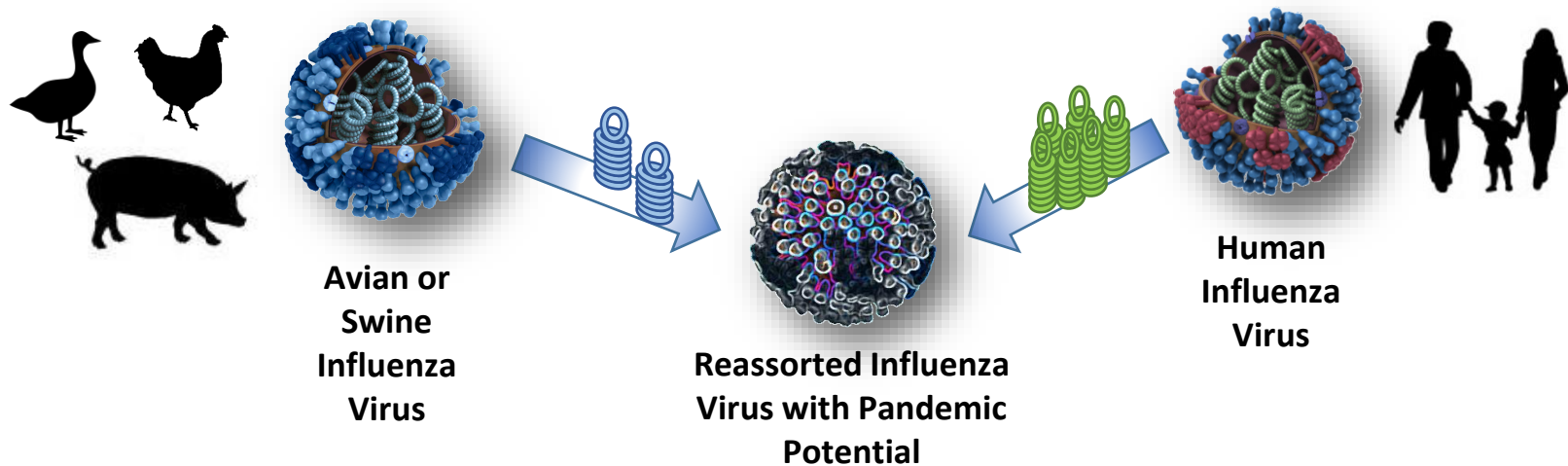


Deaths

Severe Cases
Hospitalizations

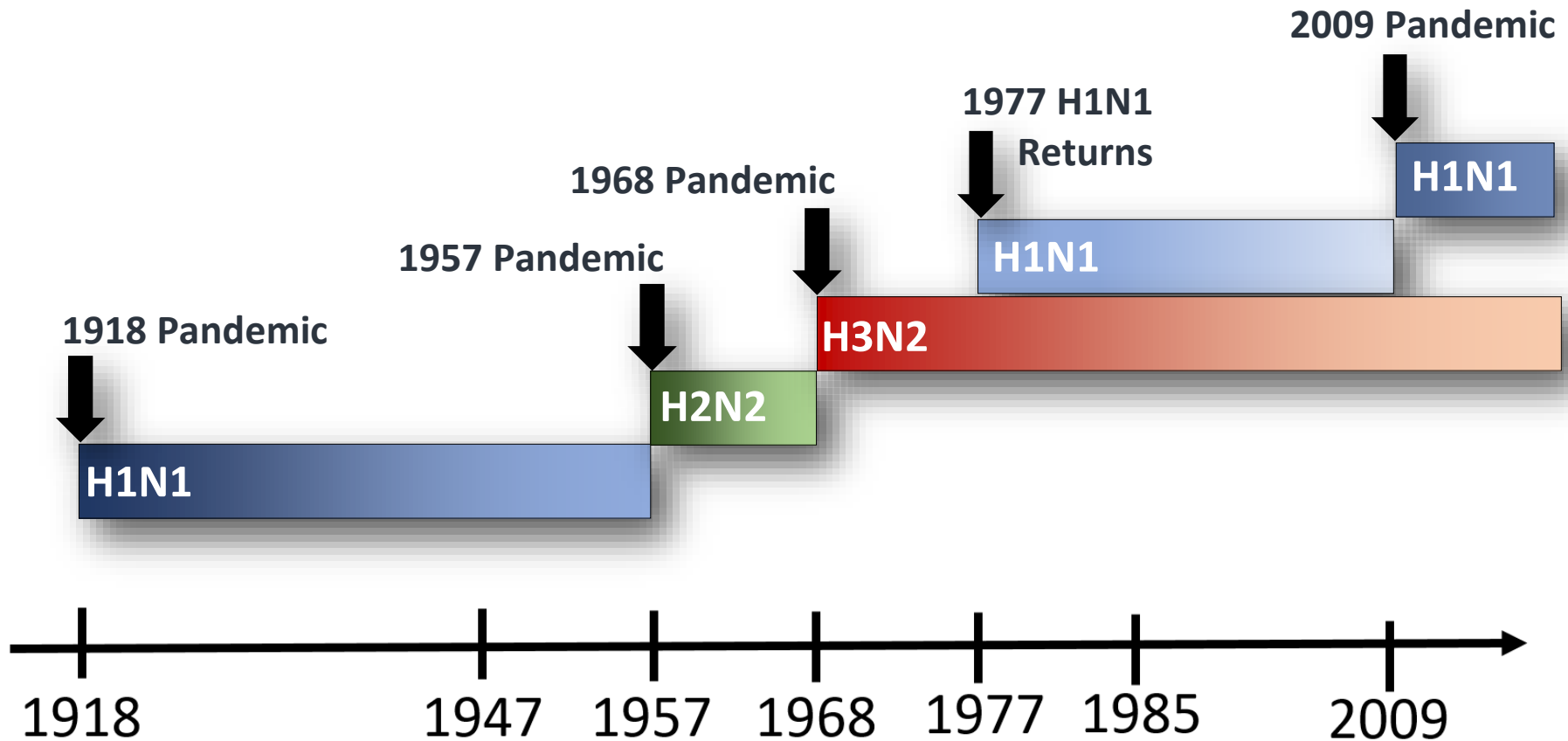
Cases

Pandemic Potential of Influenza Viruses



- Human-adapted viruses can arise from reassortment to cause efficient and sustained transmission
- Four pandemics in last 100 years

Influenza A Viruses Since 1918





The World in 1918: At War

U.S. Joins War Effort April 6, 1917

- Soldiers, food, ammunition, and money needed for war effort
- Civilian population asked to ration food, gasoline, and fabric¹
- Army Increases in Numbers
 - 378,000 in April 1917
 - >4.1 million by war's end²
 - Draft age
 - Originally 21-30
 - Expanded to 18-45 in May, 1918

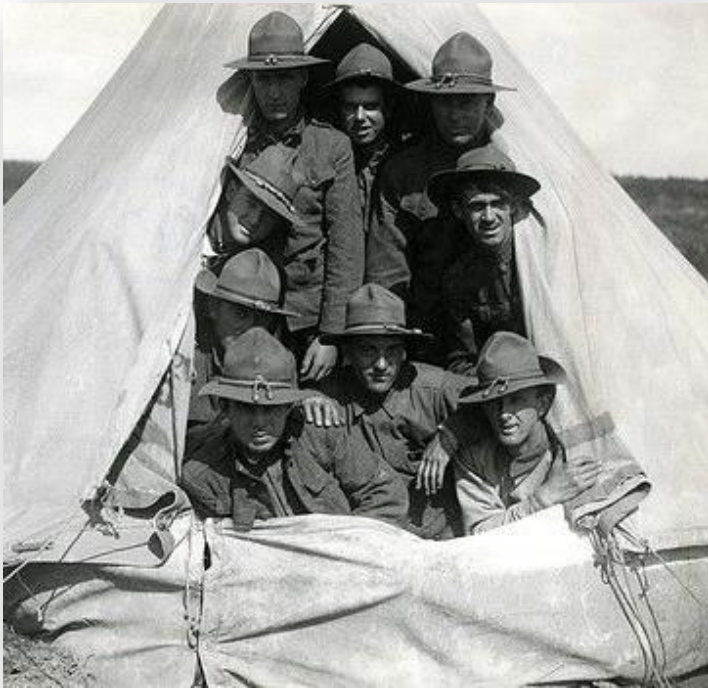


¹Navarro, 2010; ²Byerly, 2010



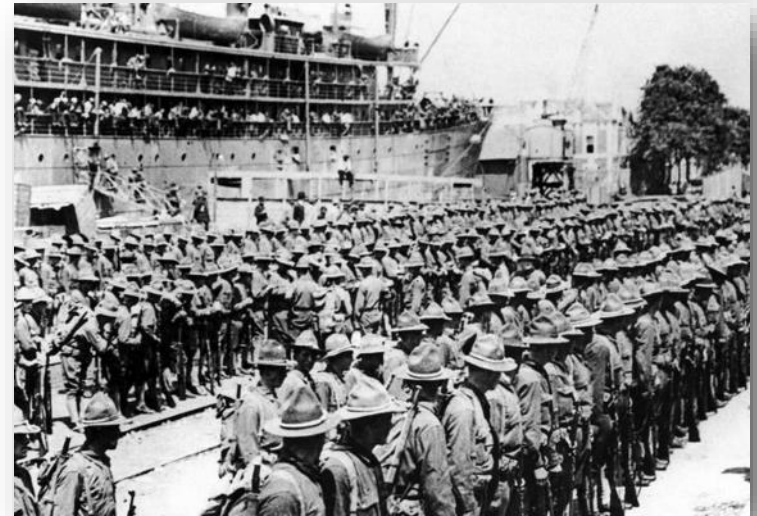
Crowding Facilitated Transmission of Infection

- Industrialization and war response added to urban overcrowding
- Soldiers in crowded camps
 - >100K in tents in US
 - 1917-18 record cold winter

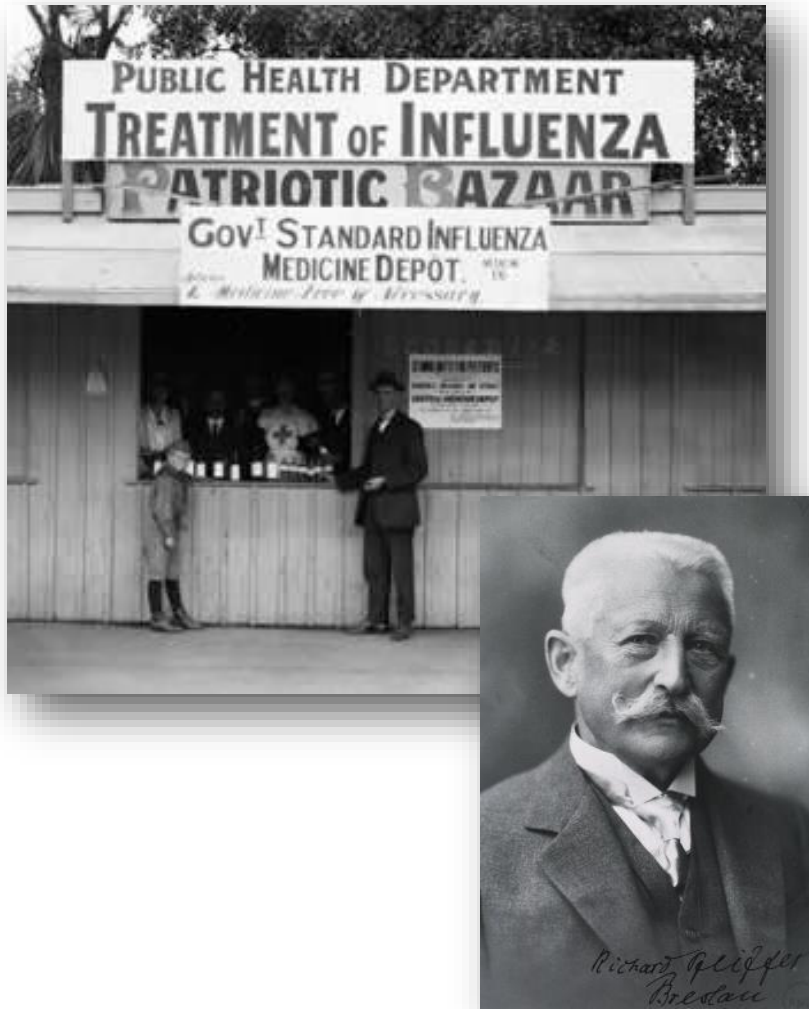


Wartime Movement Aided Transmission of Infection

- Massive troop movement
 - Immunologically-naïve young men, moved from isolated towns to training bases, and then to Europe
 - 10,000 men shipped to France every day in summer 1918
- Unprecedented troop movement allowed infection to move from camp to camp
 - JAMA in Oct 1918 reported:
 - Measles
 - Chronic Bronchitis
 - Scarlet fever
 - Pneumonia was then (and remained until 1936) the leading cause of death in the world



The Dawn of Modern Medicine



Pfeiffer

- Viruses not discovered yet, no flu treatment or prevention, flu transmission poorly understood
 - Cause of influenza attributed in 1892 by Pfeiffer to be a bacillus – *Haemophilus influenzae*
- Few vaccines:
 - typhoid, cholera, plague
- Only palliative therapies:
 - Aspirin, quinine, opium, ammonium, iodine, turpentine, beef tea

Wartime Shortage of Medical Personnel



- 30% of physicians serving in military¹
- 9,000 nurses had deployed overseas and thousands more were working in training camps²





Public Health Service



Public Health Services Officer in 1912

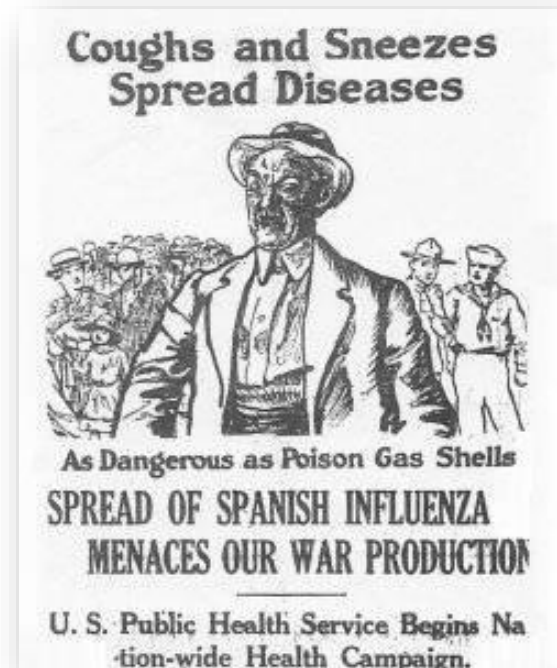
- US Public Health Service established in 1789
- When war began in 1917, President Wilson made Public Health Service part of the military



The Pandemic Begins

“Spanish” Flu

- Spain was non-combatant in WWI
- Only country to make details of their influenza experience public
- The Allied and Central Nations restricted details of their flu experience to:
 - Avoid enemy knowledge of reduced troop strength
 - Maintain morale in the population



First Published Cases in US
Public Health Reports, April 1918

PUBLIC HEALTH REPORTS

VOL. 33

APRIL 5, 1918

No. 14

April 5, 1918

502

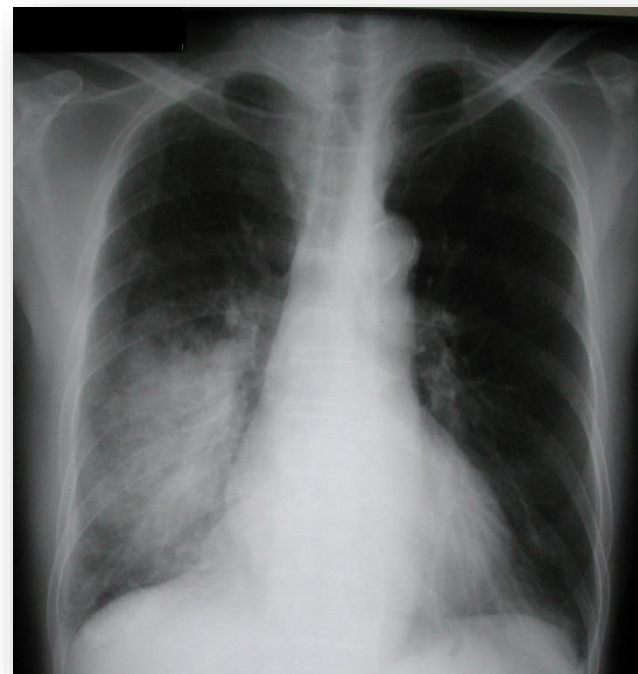
INFLUENZA.

Kansas—Haskell.

On March 30, 1918, the occurrence of 18 cases of influenza of severe type, from which 3 deaths resulted, was reported at Haskell, Kans.

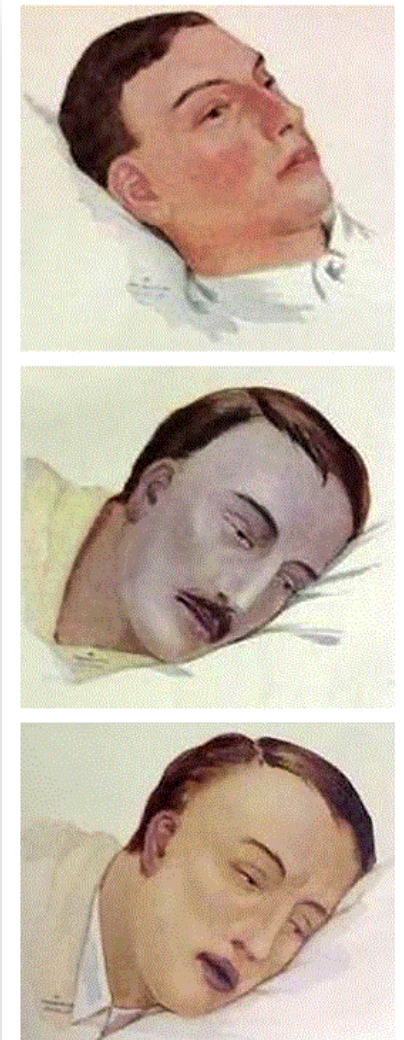
Signs and Symptoms

- Classic ILI- fever, cough, sore throat, stuffy nose, myalgia, fatigue
- Pneumonia in 10-20% of pandemic cases in Western world
 - 280,000 pneumonia deaths in healthy young adults
 - Primary viral pneumonia
 - Secondary bacterial pneumonia and empyema
- Extensive organ involvement
- Perioral cyanosis
- Death could occur quickly but typically in 3-10 days



Signs and Symptoms of 1918 Pandemic

- 'Purple Death' often in 24 hrs
 - "They very rapidly develop the most vicious type of pneumonia that has ever been seen."
 - "Cyanosis extending from their ears and spreading all over the face"
 - "It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce."
 - "Bodies stacked in the morgue from floor to ceiling like cord wood."



Figs. 1–3 Different stages of skin coloration as seen during the 1918 influenza pandemic characterized as "heliotrope" or deep blue cyanosis. Reproduced with permission from the Lancet archives.

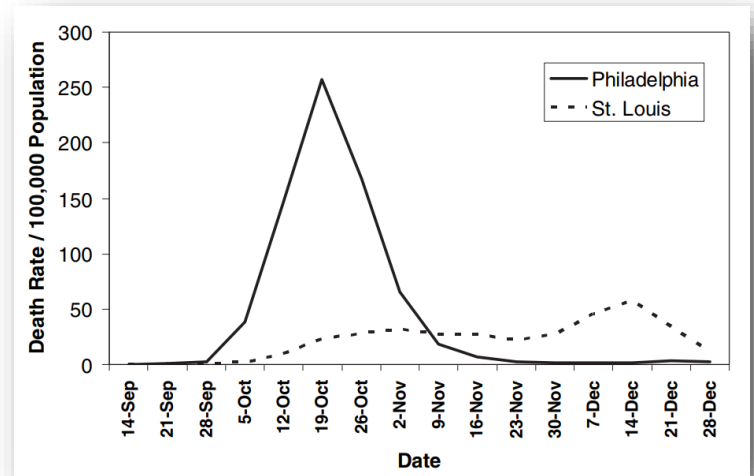
Healthcare Provider Experiences



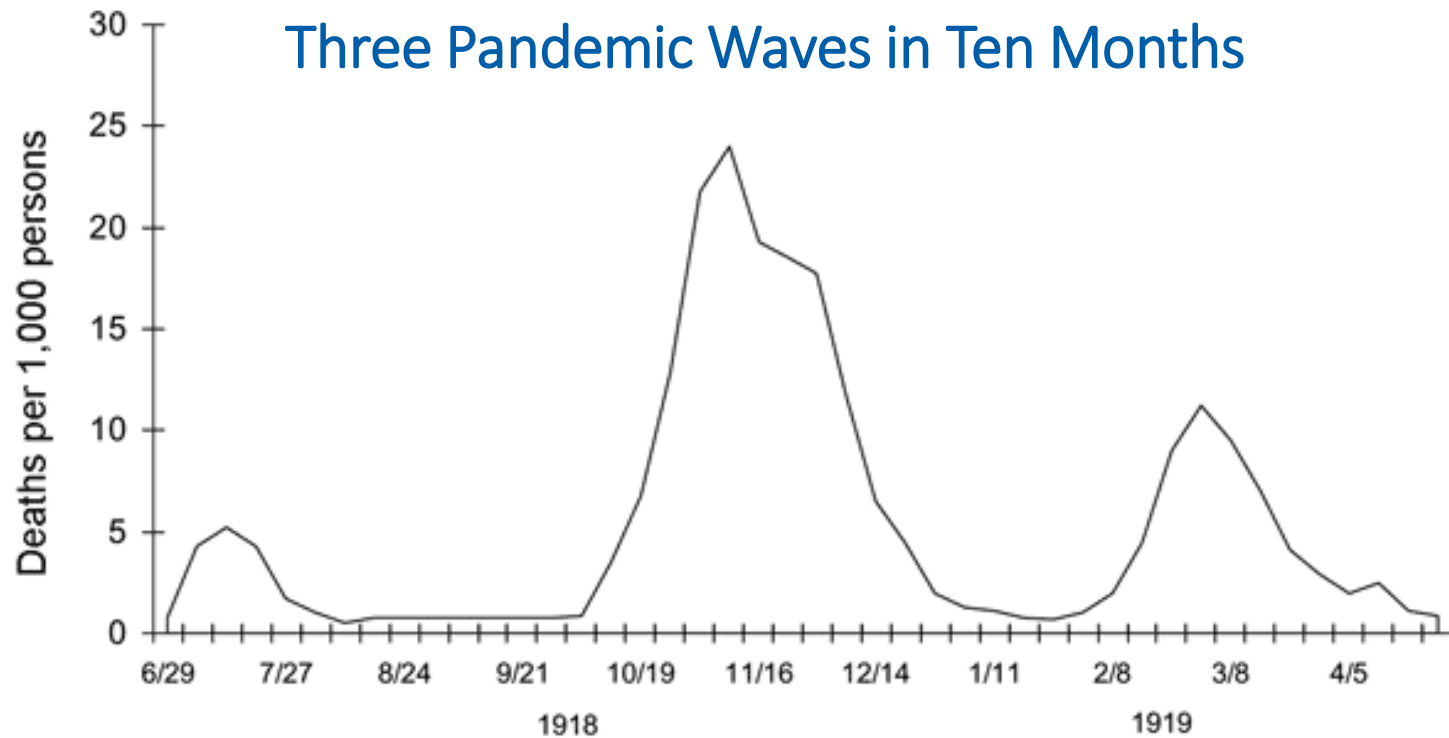
- Not uncommon to enter a home and find bodies of deceased alongside those with disease
- Some nurses were literally kidnapped during the pandemic
 - Held by force in some homes where patients were too frightened and desperate to let them leave

Effect of Community Mitigation Efforts

- Earlier timing of interventions was associated with lower peak death rates
- Interventions included:
 - Closure of schools, churches, dance halls, and theaters
 - Bans on public gatherings
- Examples from Philadelphia and St Louis
 - Philadelphia *delayed* implementation of interventions, allowed Liberty Loan Parade in September
 - St Louis implemented multiple measures *early* after first cases identified
- The difference of 14 days in response times between the two cities was approximately three to five doubling times for an influenza epidemic



Three Pandemic Waves in Ten Months



- Wave 1
 - Between February and April in North America
 - Between May and July in Europe
 - Spread across globe in less than 6 months (smallpox had taken half a century)
- Wave 2:
 - Fall (September/October)
- Wave 3:
 - Early 1919

Mortality

- Likely caused 50M deaths globally¹
- ~675,000 US deaths
 - 5 times the military losses of WWI
 - Exceeds military losses of WWI + WWII + Korea + Vietnam²
- W-shaped mortality curve showing increased rate among young- to middle-aged adults

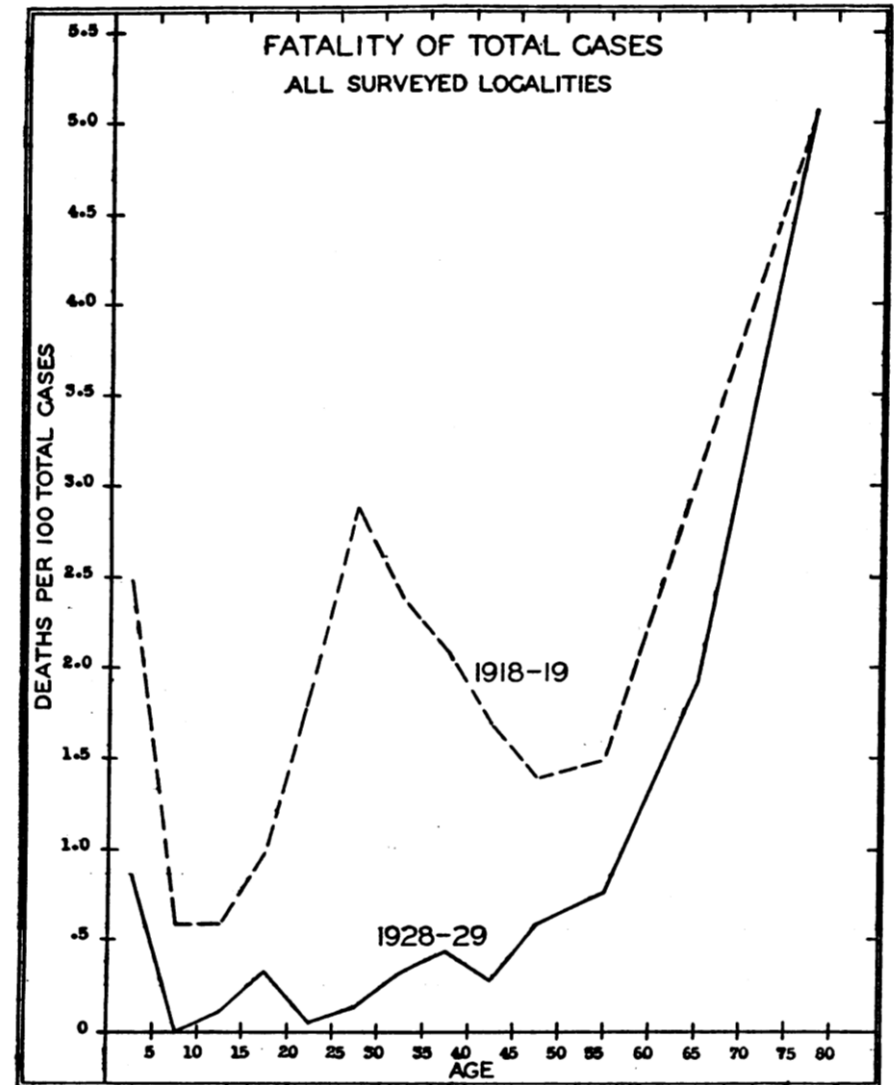
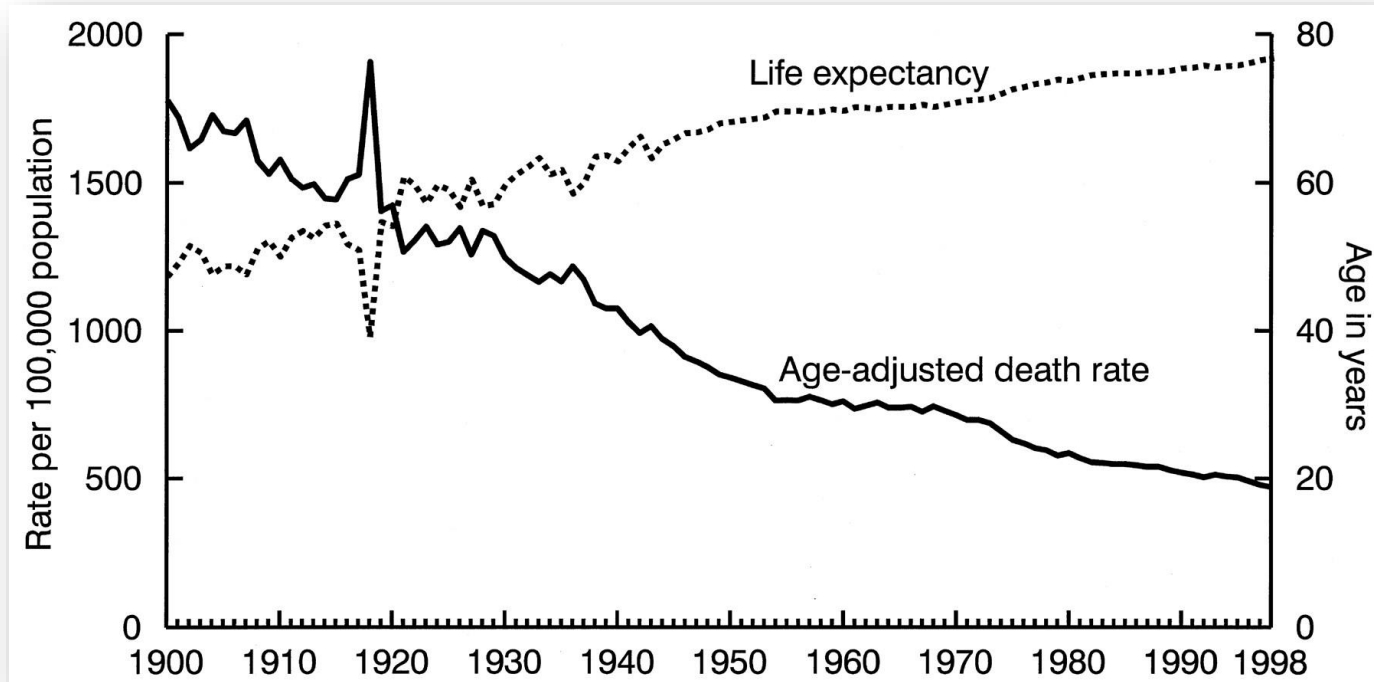


FIGURE 9.—Case fatality of respiratory illnesses among persons of different ages in surveyed groups during the epidemics of 1928-29 and 1918-19. (Respiratory cases include influenza, grippé, pneumonia, and colds with one or more days in bed)

U.S. Mortality and Life Expectancy



- Depressed overall average life expectancy by 10 – 12 years

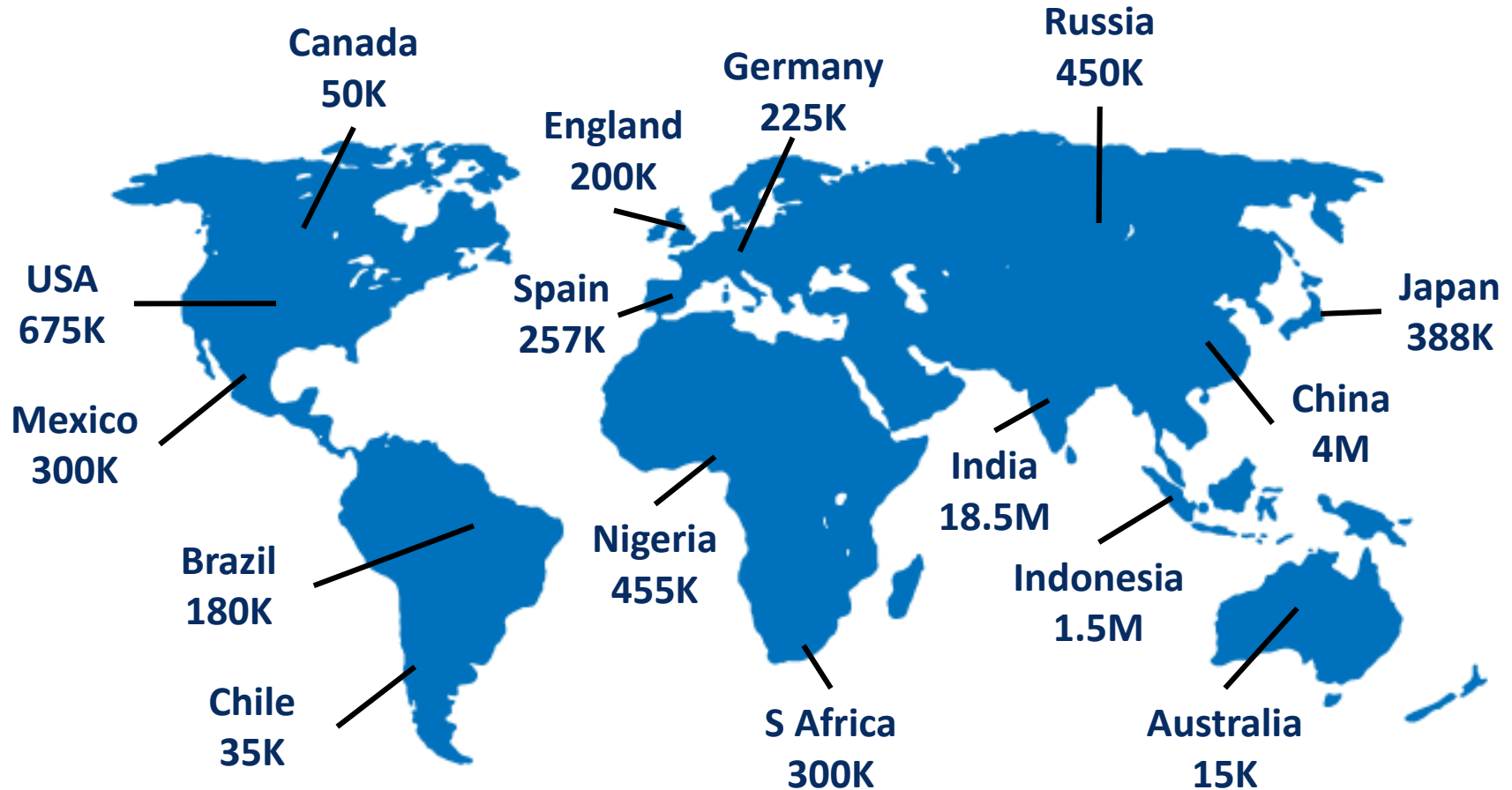


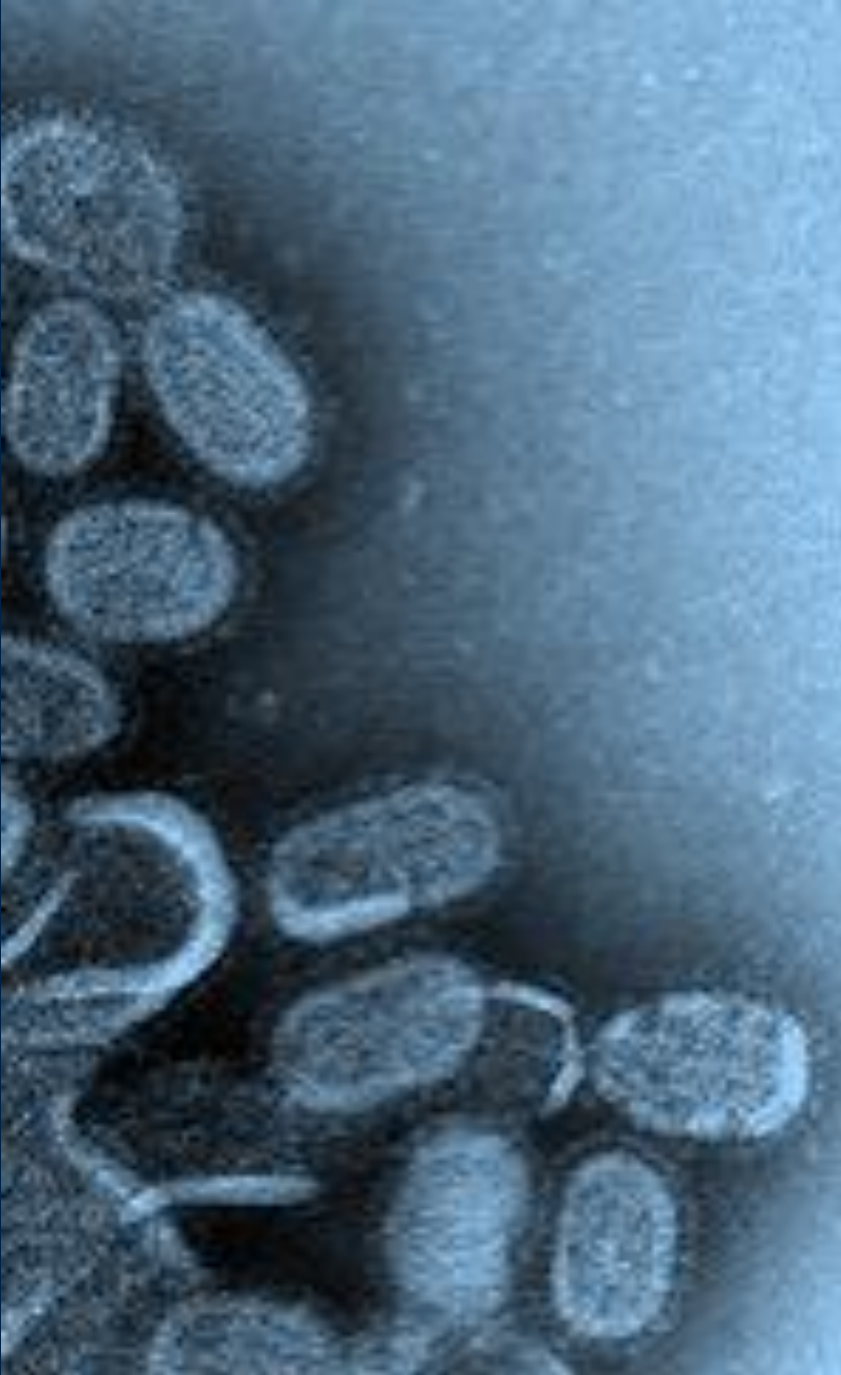
Managing the Dead

- A prominent health official gave a Midwestern official advice on how to prepare for outbreak:
 - “Begin by hunting up wood-workers, cabinet makers, and street laborers and set them to making coffins and digging graves”

Global Mortality From the 1918-1920 Pandemic

Approximately 50 Million Deaths





Evaluation of the Virus



1951

Johan Hultin at permafrost
gravesite, Brevig Mission AK

Reconstructing The 1918 Influenza Virus



1951

Johan Hultin at permafrost
gravesite, Brevig Mission AK



1951

Hultin unable to grow live
1918 virus in lab

Reconstructing The 1918 Influenza Virus



1951

Johan Hultin at permafrost gravesite, Brevig Mission AK



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1997

Hultin returns to gravesite for frozen lung tissue

Reconstructing The 1918 Influenza Virus



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Reconstructing The 1918 Influenza Virus



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2004

Tumpey at CDC rescues 1918 virus in high containment lab



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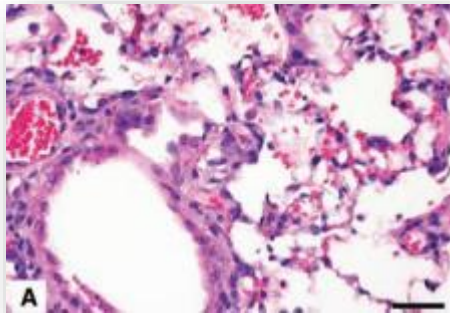


1997

Hultin returns to gravesite for frozen lung tissue



Reconstructing The 1918 Influenza Virus



2005

CDC shows 1918 virus causes severe pneumonia in mice and identifies the genes responsible for high virulence



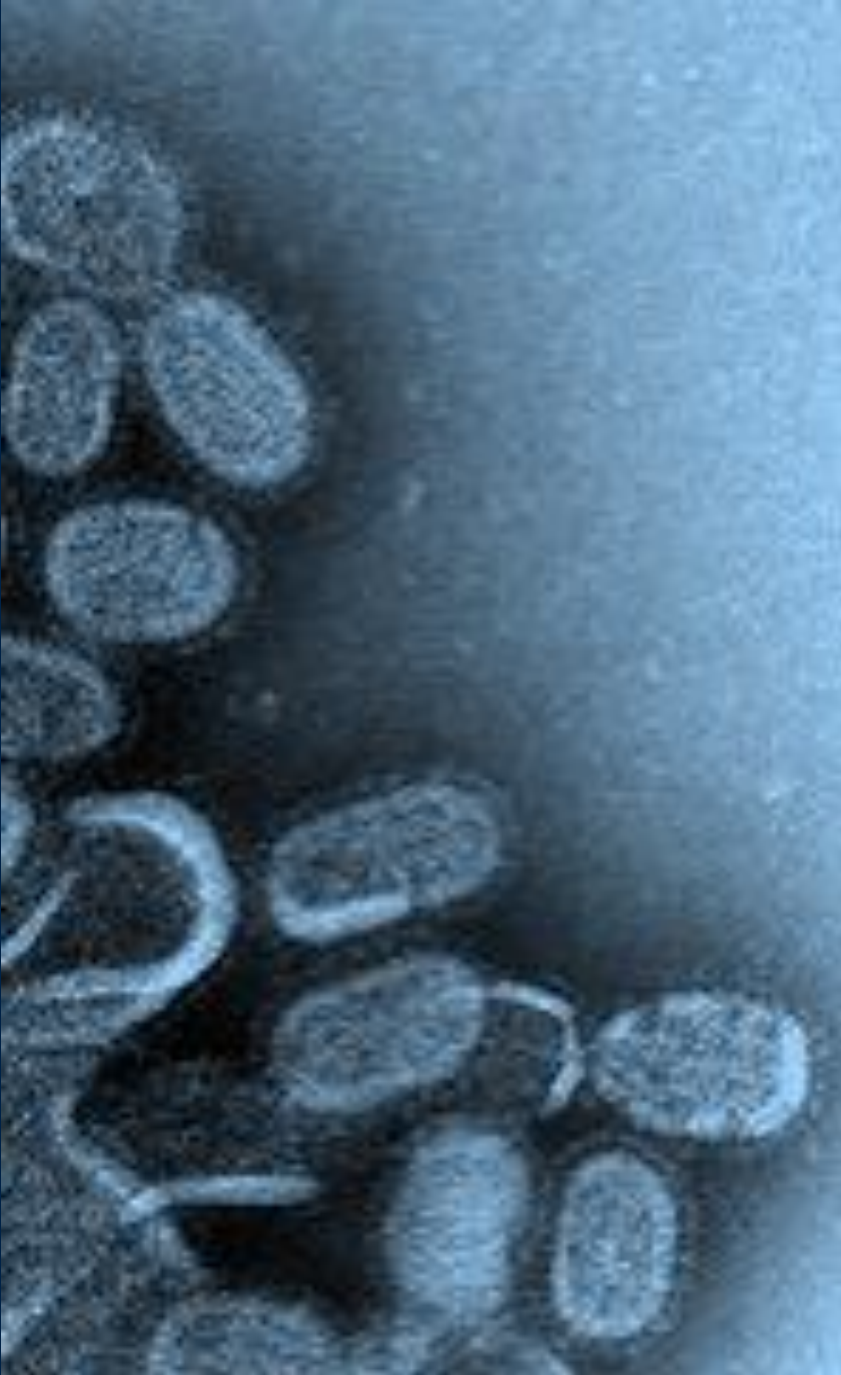
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Tumpey at CDC rescues 1918 virus in high containment lab



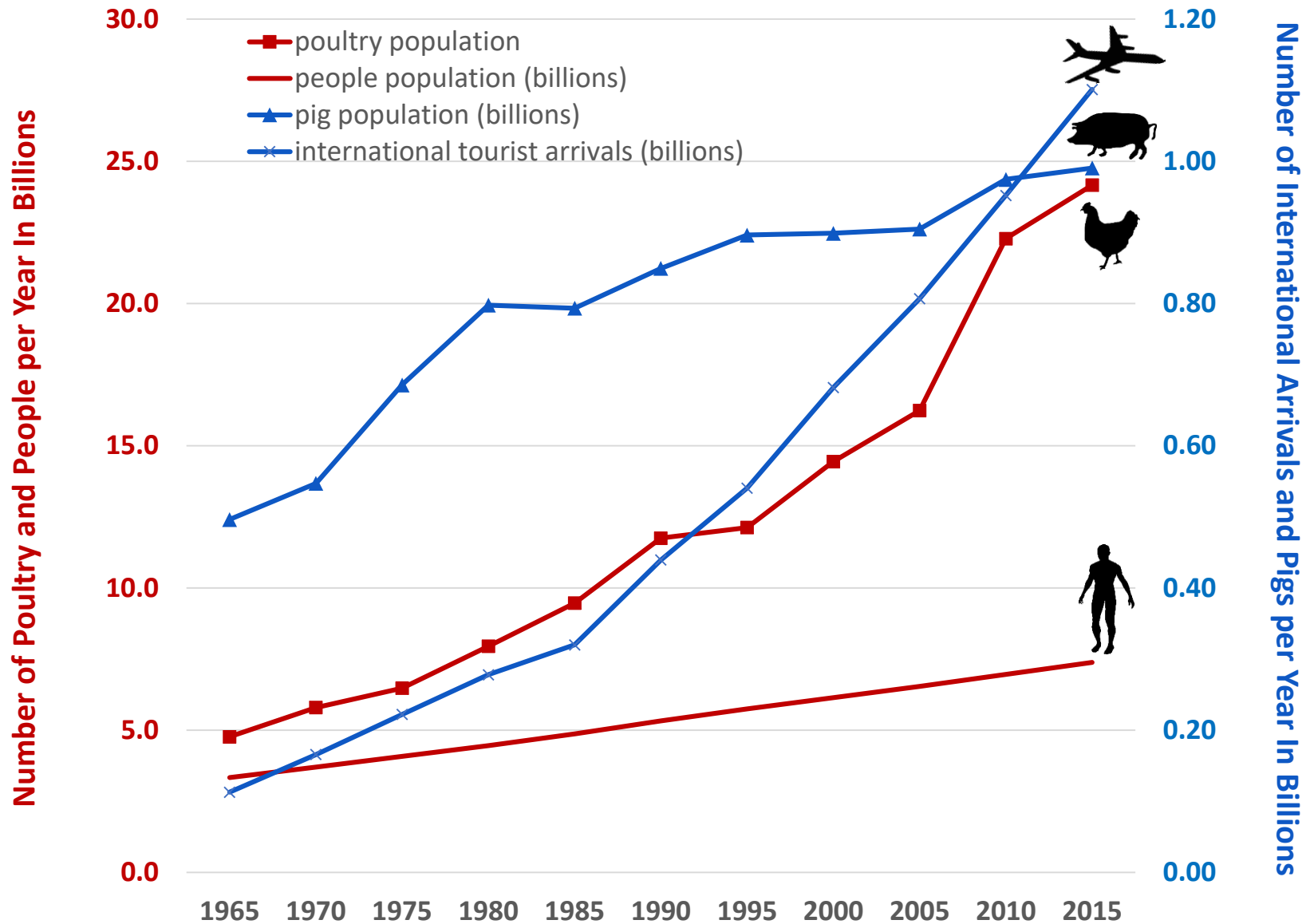
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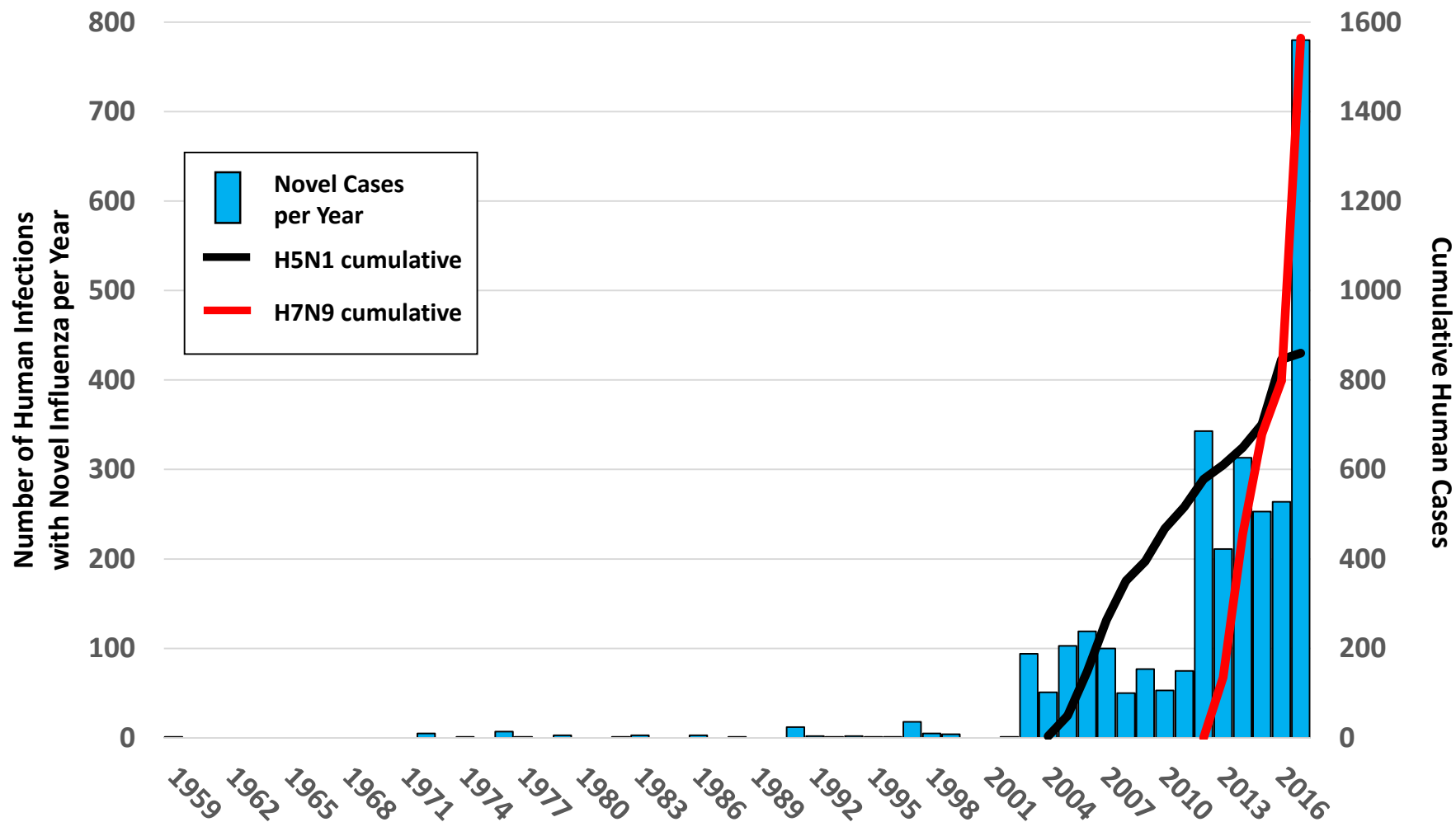


Emerging Influenza Viruses With Pandemic Potential

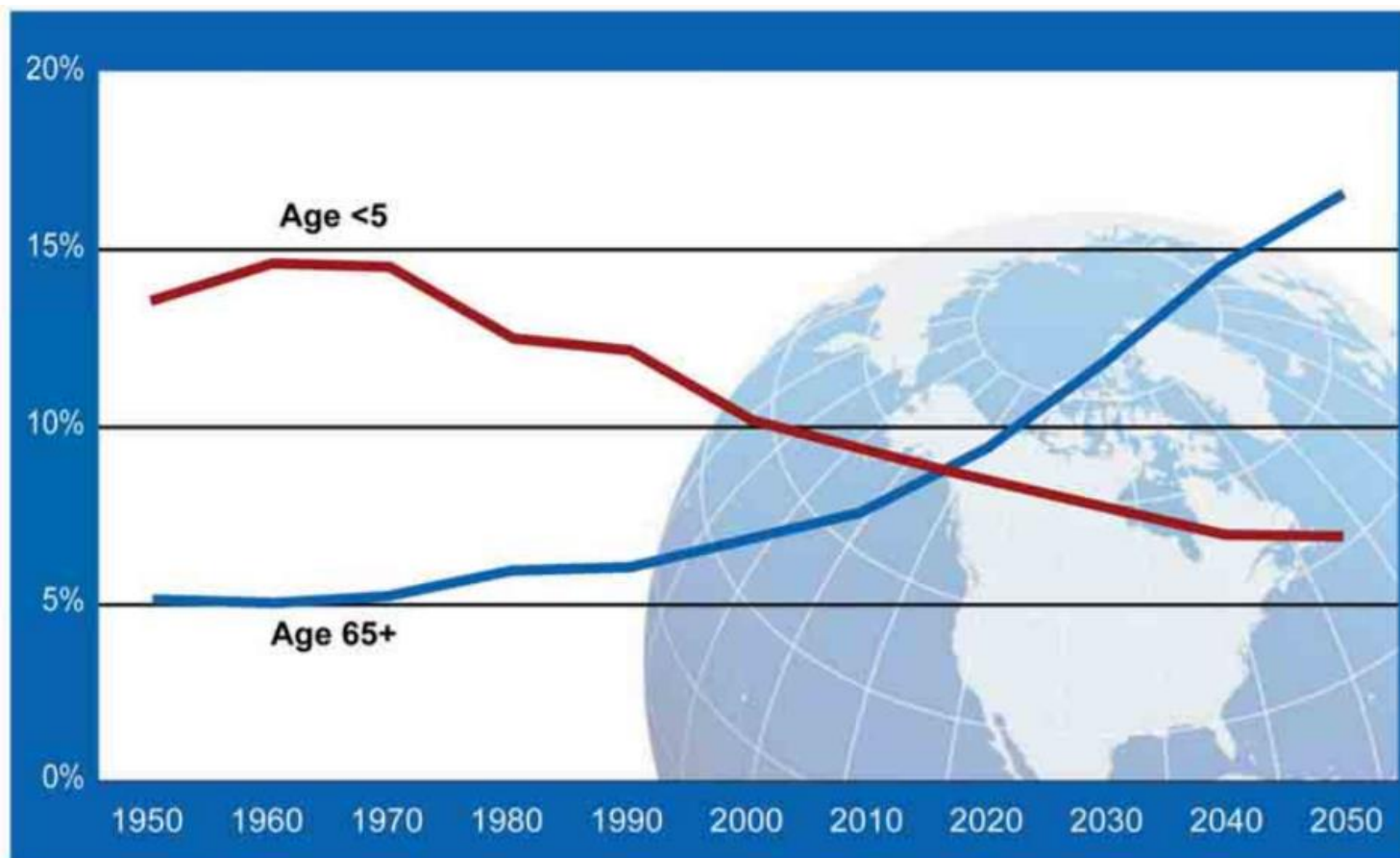
Increasing Number of Poultry, Pigs, People and Passengers 1965-2015



Increasing Number of Human Cases of Novel Influenza A Infection, 1959-2017



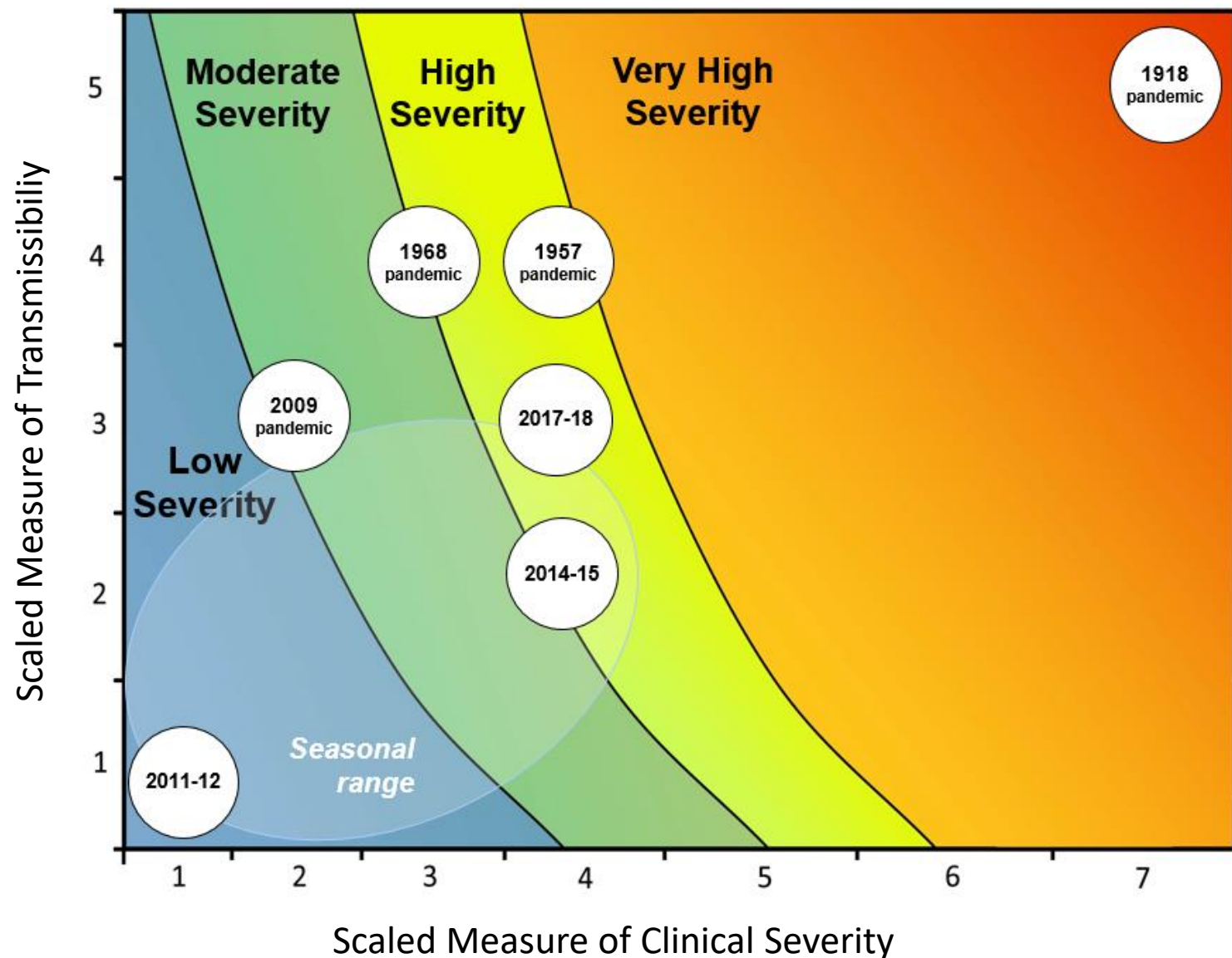
The Percentage of the Global Population Over 65 Years Of Age Is Increasing





Are We Ready For The Next Severe Influenza Pandemic?

Estimating the Impact of a 1918-Like Pandemic



Estimated Illness, Types of Medical Care, and Deaths from a Moderate to Very Severe Influenza Pandemic

Pandemic Severity (based on multiple factors ^a)	Transmissibility (% of US population ^b with clinical illness)	Illness	Outpatient medical care	Hospitalization	ICU care	Deaths
Moderate	20%	64,000,000	32,000,000	800,000	160,000	48,000
	30%	96,000,000	48,000,000	1,200,000	240,000	72,000
Severe	20%	64,000,000	32,000,000	3,800,000	1,200,000	510,000
	30%	96,000,000	48,000,000	5,800,000	1,700,000	770,000
Very Severe	20%	64,000,000	32,000,000	7,700,000	2,300,000	1,300,000
	30%	96,000,000	48,000,000	11,500,000	3,500,000	1,930,000

^a Adapted from Reed C, Biggerstaff M, Finelli L, Koonin LM, Beauvais D, Uzicanin A, Plummer A, Bresee J, Redd SC, Jernigan DB. [Novel framework for assessing epidemiologic effects of influenza epidemics and pandemics](#). Emerg Inf Dis 2013; 19:85-91.

^b [2015 US Population estimate](#) used for calculation.

If a 1918-Like Pandemic Occurred Today

- Potential disruption of transportation and supply chains
- Potential disruption of healthcare services
- Potential high economic costs
 - \$181B-\$570B estimated for moderate to severe influenza pandemic
 - SARS cost \$30 billion in only 4 months



Surveillance Readiness

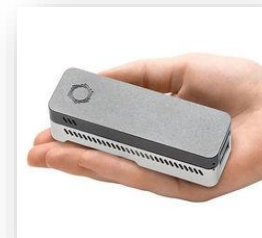
■ Strengths

- WHO Global Influenza Surveillance and Response System (GISRS)
 - 144 laboratories for virus monitoring in 113 countries
 - >400K tests reported in FluNet per year
- Next-generation sequencing of all flu viruses sent to CDC and shared with accessible public database
 - Developing field-deployable “NGS in a backpack”
- CDC supports >30 countries for surveillance and novel flu detection



■ Gaps

- ‘Data Deserts’ in Africa and Southern Hemisphere
- Inadequate surveillance in birds and swine
- Specimen sharing is too slow and complicated



Diagnostic Readiness

■ Strengths

- Global distribution of free testing materials via IRR
- CDC PCR tests detect H1, H3, B's, H5, H7 given to >140 labs globally
- Greatly improved commercial flu assays for fast PCR results



■ Gaps

- Limited flu testing and poor lab capacity in developing nations
- Difficult and slow to confirm novel flu
- Simple, reliable, OTC tests not available



Therapeutic and Clinical Readiness

■ Strengths

- Antivirals
 - Increased availability of antivirals and new monoclonal antibody (mAb) therapies in pipeline
 - FluOnCall for use in a pandemic
- Clinical Care
 - After SARS/MERS/Ebola, new facilities built for treating patients with emerging infections with high fatalities



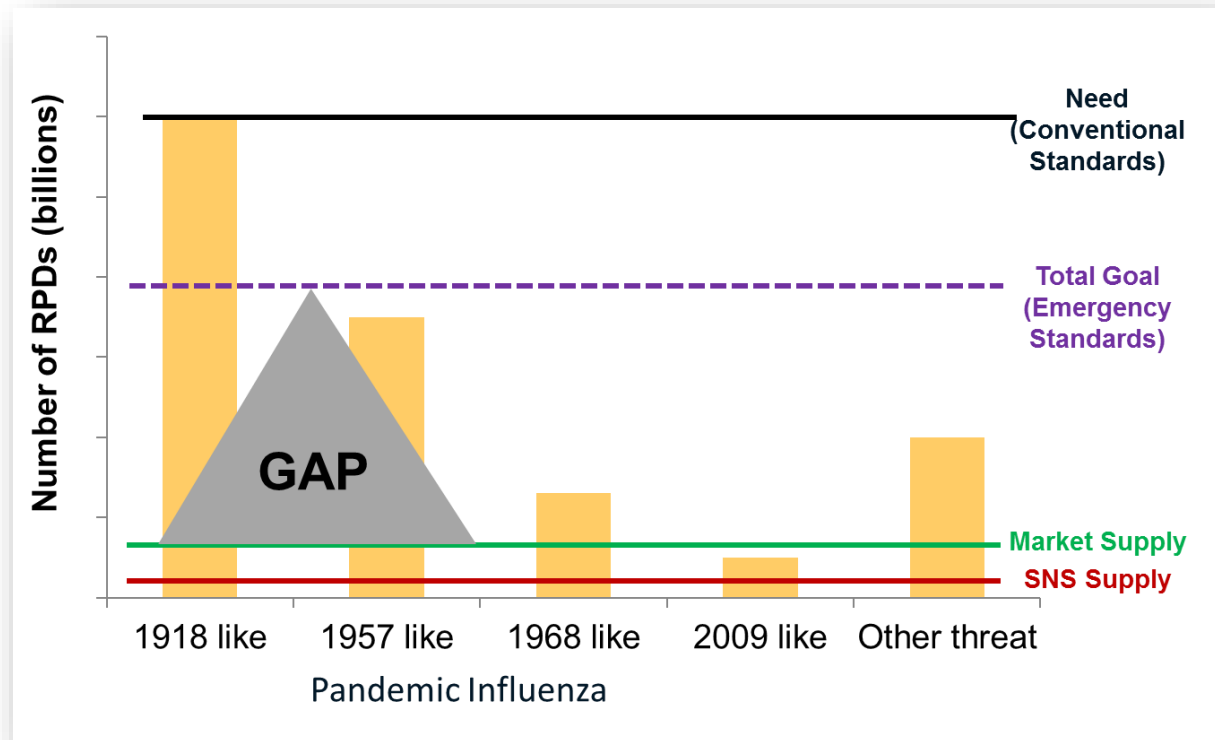
■ Gaps

- Need better performing antiviral treatment with:
 - Benefit in severe, hospitalized influenza infection
 - Greater availability and lower cost
- Need reusable respiratory protective devices
- Ventilatory and clinical support capacity is insufficient in most of globe for a severe pandemic



Respiratory Protective Devices

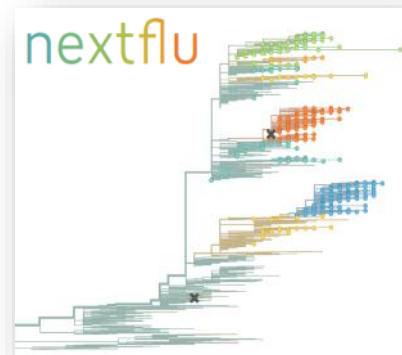
- The amount of RPD's needed for healthcare worker protection during an influenza pandemic far exceeds the amount of product available.
- Estimates:
 - Reusable RPDs: 1.62 Million
 - N95: 3,506 Million
 - Facemask: 438 Million



Vaccine Readiness

■ Strengths

- New vaccine technologies available
 - Synthetic biology for making vaccine viruses
 - Cell-grown vaccines
 - Recombinant protein vaccines
- Improved virologic forecasting
- More manufacturing capacity available
 - WHO Global Action Plan
- New programs for introducing vaccine for low- & mid-income countries



■ Gaps

- Takes too long to have vaccine available for pandemic response
- Need better current vaccines as we work toward a truly “universal” vaccine



Preparedness Planning and Response

■ Strengths

- International Health Regulations since 2005 for greater awareness and response
- WHO Pandemic Influenza Preparedness (PIP) Framework
 - Support for improving surveillance and equitable response during an influenza pandemic
 - 400 M vaccine doses anticipated for next pandemic
- Response Tools are Available
 - Pandemic Risk Assessments
 - Pandemic Severity Assessments
 - Pandemic preparedness resources

■ Gaps

- Most countries do not have robust pandemic plans and very few exercise response efforts
- Only 1/3 of countries ready for response based on IHR review

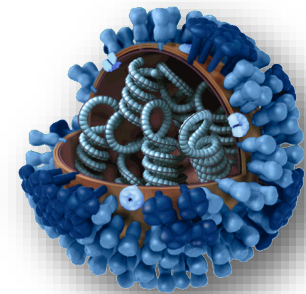


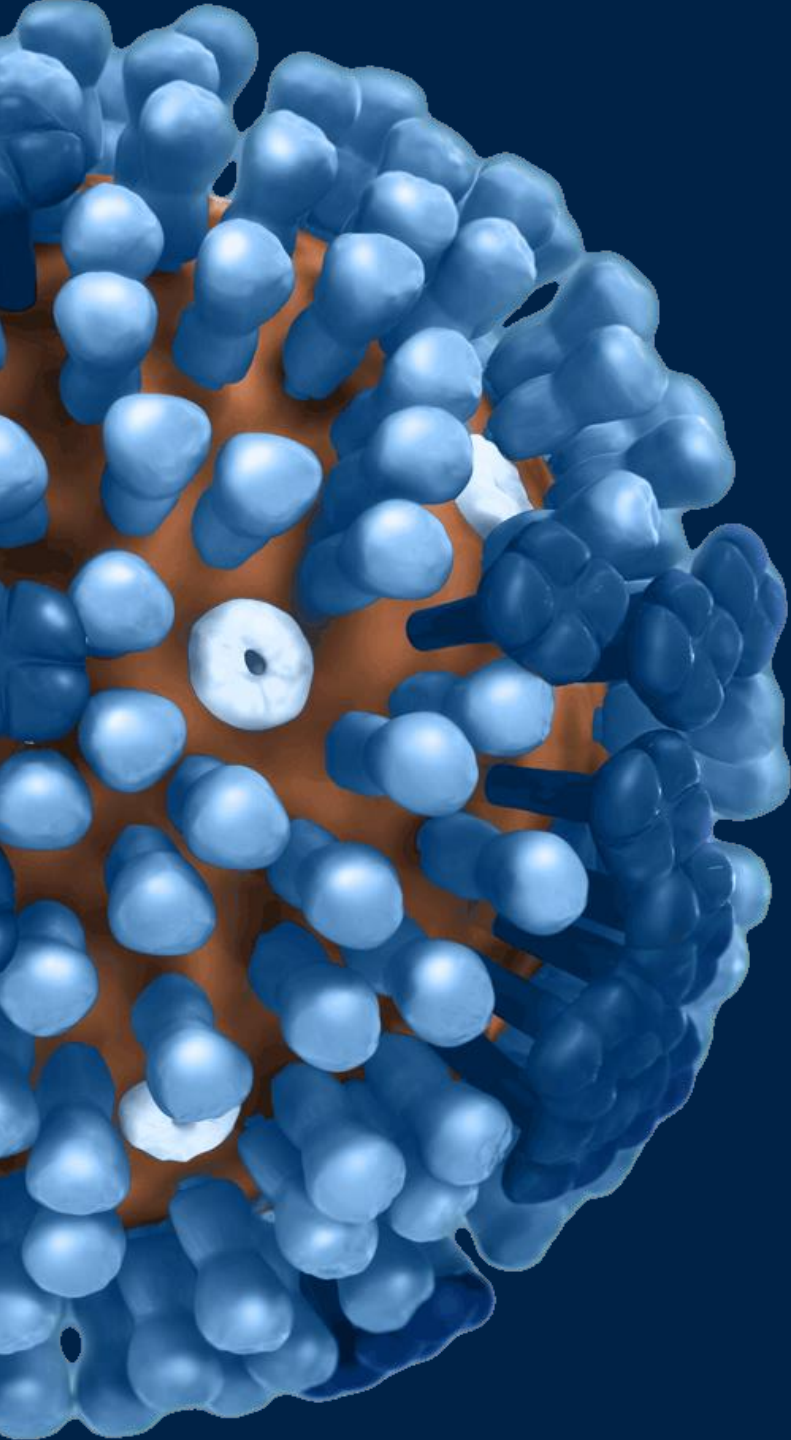
1918 and Now



Conclusions

- Seasonal influenza causes a significant burden each year, but the 1918 pandemic was exceptionally severe
 - A similar pandemic today could cause tremendous illness, death, and cost
- Number of detected emerging novel influenza viruses is increasing, necessitating ongoing laboratory surveillance and risk assessments
- Efforts to improve pandemic readiness and response are underway, however, many gaps remain
- Are we ready in 2018 for a severe influenza pandemic?
 - Better than we were, but not where we need to be.





Thank You

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WHO

GISRS

B Jester

J Katz

D Wentworth

T Tumpey

X Xu

J Barnes

B Garten

L Gubareva

T Davis

L Chen

S Lindstrom

M Levine

I York

T Maines

S Sambhara

V Dugan

D Iuliano

E Azziz-

Baumgartner

J Bresee

S Olsen

A Fry

C Reed

L Brammer

B Flannery

M Biggerstaff

A Budd

B Neuhaus

E Eisenberg

S Shepard